REMARKS

Applicants wish to thank the Examiner for the courtesy extended during an interview between the Examiner and the Applicants' attorneys wherein possible amendments to overcome the prior art were discussed.

Applicants have amended Claims 1 and 14. Support for the amendment to Claim 1 may be found for e.g., in original Claim 1 and throughout the application. Claim 14 has been amended to correct typographical errors. It is submitted that no new matter has been introduced by the present amendments and entry of the same is respectfully requested.

By these amendments, the Applicants do not acquiesce to the propriety of any of the Examiner's rejections and do not disclaim any subject matter to which they are entitled.

Obviousness Rejections under 35 U.S.C. §103 should be withdrawn

1. Claims 1-16, 18 & 20-24 are rejected under 35 U.S.C 103(a) as allegedly being unpatentable over Urdea *et. al.* (1989, "Urdea") in view of Lockhart *et. al.* (2000, "Lockhart"). Applicants respectfully disagree with the Examiner. However, for the purpose of expediting the issuance of claims, Applicants have amended Claim 1 to recite "at least 50 mediator nucleic acids and at least 50 different cipher probes immobilized on a microarray" etc.

Urdea discuss methods for detecting a **single** analyte using two sets of probes, a binding probe (B, figure 1) and a label probe (A, figure 1). A target is bound by multiple probes in multiple regions (Figure 1). Applicants reiterate that no methods for detecting

multiple analytes are disclosed in Urdea. In contrast, Claims 1-16, 18 & 20-24 recite methods for "detecting a plurality of at least 50 different nucleic acid targets." Lockhart teach expression monitoring on high density arrays with bound oligonucleotide arrays in which more than 100 different oligonucleotides may be bound. The primary advantage of the Claimed methods, however, is the flexibility of the assay, i.e., one type of array can be used as a universal array to detect different sets of targets by using different mediator probes. In addition, adding a large number of mediator probes increases the complexity of microarray-based assays and places the Claimed methods much above the level of one of ordinary skill in the art.

The Office Action alleges that one of skill in the art would be motivated to combine Lockhart's multiple probes and lengths to Urdea's assay in order to detect a multiplicity of genes and provide a high throughput analysis of multiple genes with high signal to noise ratio. Applicants respectfully submit that this objection has been overcome by the above amendments and arguments. Therefore, this rejection of Claims 1-6, 18 and 20-24 should be withdrawn.

2. Claims 17 and 19 are rejected under 35 USC 103(a) as allegedly being unpatentable over Urdea in view of Lockhart and further in view of Vinayak *et. al.* (2001, "Vinayak"). For the above reasons, applicants respectfully submit that it is not prima facie obvious to use mediator and cipher probes to detect multiple analytes on a microarray substrate. Therefore, this rejection of Claims 17 and 19 should also be withdrawn.

3. Claims 1-16, 18 and 20-24 are rejected under 35 USC 103(a) as allegedly being unpatentable over Southern *et. al.* (2000, "Southern") in view of Lockhart. Applicants respectfully disagree with the Examiner. Southern discuss a method of detecting targets

with an ASO probe bound to a support and an intermediate polynucleotide which binds to the bound ASO probe and another target, that ultimately leads to ligation. The Examiner alleges that one of ordinary skill in the art would have been motivated to apply Lockhart's teachings of 100 different oligonucleotides to Southern's method of analyzing sequences in order to detect multiple samples.

Applicants respectfully submit that Southern does not teach "at least 50 different mediator and cipher probes." Moreover, neither Lockhart nor Southern, alone, or in combination, capture the flexibility of the present assay where a universal array can be used to detect different sets of targets. Therefore, this objection to Claims 1-16, 18 and 20-24 should be withdrawn.

4. Claims 17 and 19 are rejected under 35 USC 103(a) as allegedly being unpatentable over Southern in view of Lockhart and further in view of Vinayak. For the above reasons, applicants respectfully submit that it is not prima facie obvious to use mediator and cipher probes to detect multiple analytes on a microarray substrate. Therefore, this rejection of Claims 17 and 19 should also be withdrawn.

Claim Rejections under 35 U.S.C. §112 are obviated

Claims 1-24 are rejected under 35 U.S.C. 112, second paragraph as allegedly being indefinite since the term "the mediator nucleic acids" lacks antecedent basis. Applicants have amended Claim 1 to address this objection.

CONCLUSION

For these reasons, Applicants believe all pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

If the Examiner has any questions pertaining to this application, the Examiner is requested to contact the undersigned attorney.

Respectfully submitted,

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